

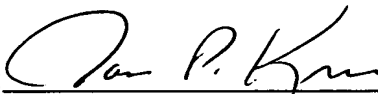
Group VI, claim(s) 1-5 and 14-16, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a oxazocine ring.

Group VII, claim(s) 7-8 and 14-41, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a morpholine ring.

Applicant hereby elects the claims of Group II, claim(s) 1-40, drawn to compounds, compositions, process of preparing and method of use of the compounds of formula I where E is a piperidine ring for continued prosecution.

Respectfully submitted,

FITCH, EVEN, TABIN & FLANNERY

By: 

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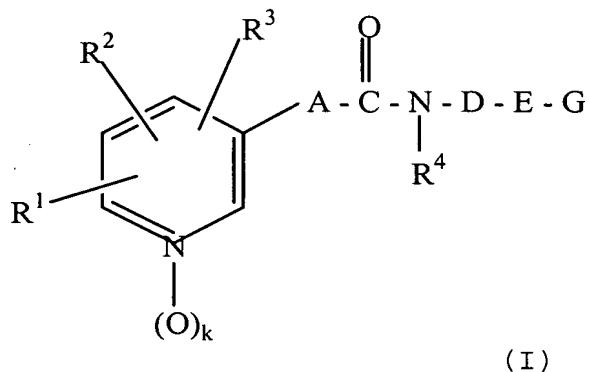
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Biedermann et al.)
)
Serial No.: 09/242,540)
)
Filed: February 18, 1999)
)
Title: PYRIDYL ALKENE AND)
PYRIDYL ALKINE-ACID)
AMIDES AS CYTOSTATICS AND)
IMMUNOSUPPRESSIVES)
)
Group Art Unit: 1624)
)
Examiner: B. Coleman)
)
)

Version with Markings to Show Changes Made

Honorable Commissioner of Patents
and Trademarks
ATTENTION: Assistant Commissioner
for Patents
Washington, D.C. 20231

42. (once amended) A compound of formula (I) and
pharmaceutically acceptable salts of formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, [C₁] C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, [and] NR⁵R⁶, and bridged R¹R² wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl; [,] and

R⁶ is [are selected independently from each other] selected from the group consisting of hydrogen and C₁-C₆-alkyl; [,]

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

wherein

[R¹ and R², in the case they] bridged R¹R² is where R¹R² are adjacent[, optionally] and form a bridge which is selected from the group consisting of -(CH₂)₄-, (CH=CH)₂- and -CH₂O-CR⁷R⁸-O-_i [,] wherein

R⁷ is selected from the group consisting of hydrogen, and C₁-C₆-alkyl; and

R⁸ [are, independent from each other,] is selected from the group consisting of hydrogen [or] and C₁-C₆-alkyl; [,]

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl; [,]

R⁴ is selected from the group consisting of hydrogen, C₁-

C₆-alkyl, C₃-C₆-alkenyl, hydroxy, C₁-C₆-alkoxy and benzyloxy_i [,]

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene, [which is optionally]

a substituted C₂-C₆-alkenylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano, or phenyl,

C₄-C₆-alkadienylene, [which is optionally]

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene, [which is optionally]

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, or cyano, and ethynylene_i [,]

D is selected from the group consisting of

C₁-C₁₀-alkylene, [optionally]

a substituted C₁-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

C₂-C₁₀-alkenylene, [optionally]

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond [optionally] is to [ring] E,

C₃-C₁₀-alkynylene, [optionally]

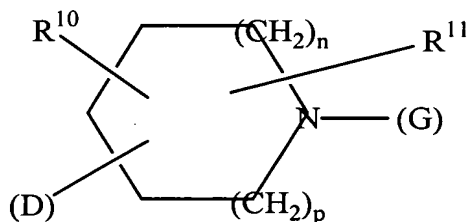
a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, [and]

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, [wherein] the isosterically replaced C₁ to

C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂;[,] wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;[,]

E is



[(E1)],

wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, or 3, [with the proviso that] wherein **n + p** [= 2] ≤ 3,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;[,]

R¹¹ is selected from the group consisting of hydrogen [or] and an oxo group adjacent to the nitrogen atom in E;[,].

G is selected from the group consisting of hydrogen,
G1, G2, G3, G4 and G5;[,] wherein

G1 [represents the residue] is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$ [(G1)]
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R^{12} is selected from the group consisting of

hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered

heterocycles[,] which heterocycles contain one to three
hetero-atoms selected from the group consisting of N, S and O,
[and are the N, S and O being] which heterocycles are either
bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system[s] with 8 to 16 ring
atoms and at least one aromatic ring[, wherein the bond
occurs] and the carbocyclic ring and aromatic ring being
bonded with a bond which is either over an aromatic or a
hydrogenated ring and either directly or over a methylene
group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring systems with 8 to 16

ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from N, S and O and the carbocyclic ring and aromatic ring being bonded with a bond which is [the bond occurs] either over an aromatic or a hydrogenated ring, and either directly or over a methylene group; [,]

R^{13} has the same meaning as R^{12} , but is selected independently thereof,

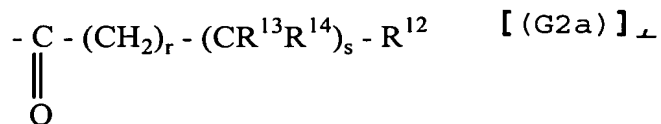
R^{14} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, monocyclic aromatic five- and six-membered heterocycles[,] which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system[s] with 8 to 16 ring atoms and at least one aromatic ring[, wherein the bond occurs] and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group; and

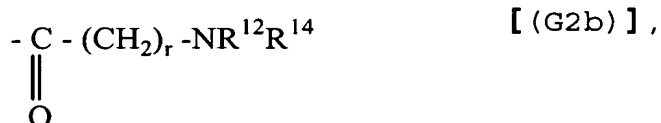
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system[s] with 8 to 16 ring atoms and at least one aromatic ring, [wherein] which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is [bond occurs either] over an aromatic or a hydrogenated ring and either directly or over a

methylene group; [,]

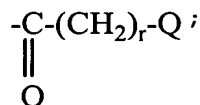
G2 is selected from the group consisting of



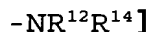
[and]



and



wherein R¹² and R¹⁴ have the above meaning, and Q [or the group



is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

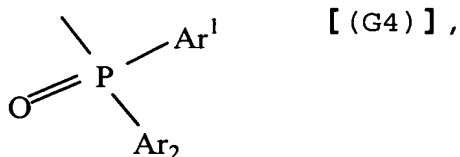
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from [the] an essential nitrogen atom[, optionally] contain one or two further heteroatoms selected from N, S and O, [and the group consisting of]

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from [the] an essential nitrogen atom[, optionally] contain one or two further hetero-atoms selected from N, S and O,

G3 is [the residue] $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{12}$ [(G3)],

G4 is [the residue]



wherein

Ar^1 is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar^2 [are selected independently of each other] is selected from the group consisting of phenyl, pyridyl and naphthyl; [,]

G5 is [the residue] $-\text{COR}^{15}$ [(G5)],

wherein

R^{15} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy and benzyloxy; [,] and

wherein aromatic [ring systems] rings in [the substituents] R^1 , [R^2 ,] R^4 , R^{12} , R^{13} , R^{14} , R^{15} , Q, Ar^1 and Ar^2 [and in the ring system $-\text{NR}^{12}\text{R}^{14}$ optionally carry independently of

each other] are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is [optionally] entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of [the] an aromatic ring in the substituted C1-C6 alkoxy [or ring system optionally] may form an additional ring over a methylenedioxy bridge, [stereoisomers and/or mixtures thereof and pharmacologically acceptable acid addition salts with the exception of] wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide [hydrochloride].

43. (once amended) A compound according to claim 42, wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, C₁-C₄-alkoxy, ethylthio, methoxycarbonyl, tert-butoxycarbonyl, aminocarbonyl, carboxy, and phenoxy,

R² is selected from the group consisting of hydrogen, halogen, trifluoromethyl and hydroxy,

R³ is hydrogen or halogen,

R⁴ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy and C₁-C₃-alkoxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene, [optionally]

a substituted C₂-C₆-alkenylene which is substituted once or twice by C₁-C₃-alkyl, hydroxy or fluorine,

a C₄-C₆-alkadienylene, [optionally]

a substituted C₄-C₆-alkadienylene which is substituted by C₁-C₃-alkyl or by 1 or 2 fluorine atoms, [and]

1,3,5-hexatrienylene, [optionally] and

a substituted 1,3,5-hexatrienylene which is substituted by fluorine,

D is selected from the group consisting of C₁-C₈-alkylene, [optionally]

a substituted C₁-C₈-alkylene which is substituted once or twice by methyl or hydroxy,

C₂-C₈-alkenylene, [optionally]

a substituted C₂-C₈-alkenylene which is substituted once or twice by methyl or hydroxy,

an E double bonded substituted C₂-C₈-alkenylene which has a double bond [wherein the double bond optionally is] to ring E,

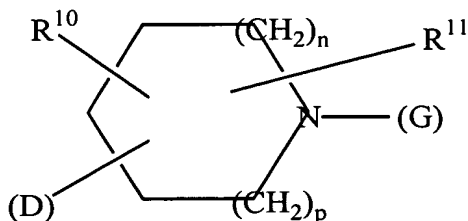
C₃-C₈-alkynylene, [optionally]

a substituted C₃-C₈-alkynylene which is substituted once or twice by methyl or hydroxy, and

an isosterically replaced C₁ to C₈ group selected from the group consisting of C₁-C₈-alkylene, C₂-C₈-alkenylene and C₃-C₈-alkynylene, the isosterically replaced C₁ to C₈ group having methylene units and [in which] one to three methylene units are isosterically replaced by O, S, NH, N(CH₃),

N(COCH₃), N(SO₂CH₃), CO, SO or SO₂,

E is



wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, or 3, [with the proviso that] wherein **n + p** [= 2] ≤ 3,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;[,]

R¹¹ is selected from the group consisting of hydrogen [or] and an oxo group adjacent to the nitrogen atom in E;[,]

G is selected from the group consisting of hydrogen, G1, G2, G3, G4 and G5;[,]

 wherein

G1 [represents the residue] is -(CH₂)_r-(CR¹³R¹⁴)_s-R¹² [(G1)] wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₈-cycloalkyl, benzyl, phenyl, [the group consisting of] benzocyclobutyl, indanyl, indenyl, oxoindanyl, naphthyl,

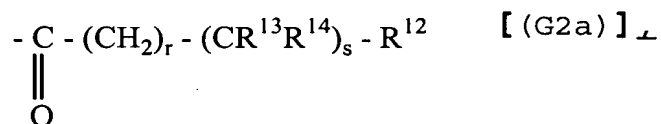
dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl,
 biphenylenyl, fluorenyl, oxofluorenyl, anthryl,
 dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl,
 phenanthryl, dihydrophenanthryl, oxodihydrophenanthryl,
 dibenzocycloheptenyl, oxodibenzocycloheptenyl,
 dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl,
 dihydrodibenzocyclooctenyl, tetrahydrodibenzocyclooctenyl and
 oxotetrahydrodibenzocyclooctenyl, bound directly or over a
 methylene group, [and the group consisting of] furyl, thienyl,
 pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl,
 pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl,
 pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl,
 imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl,
 dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl,
 dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl,
 benzisoxazolyl, oxobenzisoxazolyl, benzothiazolyl,
 oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl,
 benzimidazolyl, oxobenzimidazolyl, indazolyl,
 oxoindazolyl, benzofurazanyl, benzothiadiaazolyl,
 benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl,
 thiazolopyridyl, oxodihydrothiazolopyridyl,
 isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl,
 pyrazolopyridyl, oxodihydropyrazolopyridyl, thienopyrimidinyl,
 chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl,
 isoquinolyl, dihydroquinolyl, oxodihydroquinolyl,
 tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl,
 quinoxalyl, quinazolyl, naphthyridyl, carbazolyl,
 tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl,
 acridinyl, oxodihydroacridinyl, phenothiazinyl,
 dihydrodibenzoxepinyl, oxodihydrodibenzoxepinyl,
 benzocycloheptathienyl, oxobenzocycloheptathienyl,
 dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl,
 dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl,
 octahydrodibenzothiepinyl, dihydrodibenzazepinyl,
 oxodihydrodibenzazepinyl, octahydrodibenzazepinyl,

benzocycloheptapyridyl, oxobenzocycloheptapyridyl, dihydropyridobenzodiazepinyl, dihydrodibenzoxazepinyl, dihydropyridobenzoxepinyl, dihydropyridobenzoxazepinyl, oxodihydropyridobenzoxazepinyl, dihydrodibenzothiazepinyl, oxodihydrodibenzothiazepinyl, dihydropyridobenzothiazepinyl, and oxodihydropyridobenzothiazepinyl, bound directly or over a methylene group,

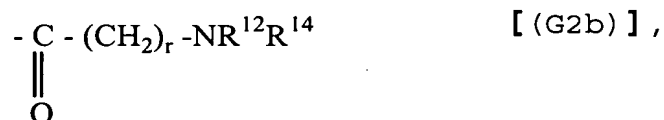
R¹³ has the same meaning as **R¹²**, but is selected independently therefrom,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, [and, the group consisting of] indanyl, indenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, triazinyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl, and tetrahydroquinolyl, bound directly or over a methylene group,

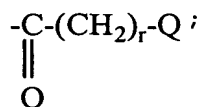
G2 is selected from [the residues] the group consisting of



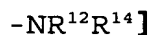
[and]



and



wherein R^{12} and R^{14} have the above meaning, and Q [or the group

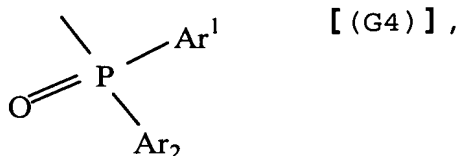


is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of azetidine, pyrrolidine, piperidine, (1H)tetrahydropyridine, hexahydroazepine, (1H)tetrahydroazepine, octahydroazocine, pyrazolidine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, thiomorpholine, thiomorpholine-1,1-dioxide, 5-aza-bicyclo[2.1.1]hexane, 2-aza-bicyclo[2.2.1]heptane, 7-aza-bicyclo[2.2.1]heptane, 2,5-diaza-bicyclo[2.2.1]heptane, 2-aza-bicyclo[2.2.2]octane, 8-aza-bicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, 9-azabicyclo[3.3.1]nonane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[c]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (10H)-phenoxazine, (10H)-phenothiazine, (5H)-dibenzazepine, (5H)-dihydrodibenzazepine, (5H)-octahydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-

dihydrodibenzo[b,f]oxazepine, (10H) -
dihydrodibenzo[b,f]thiazepine, and
(5H) -tetrahydrodibenzazocine,

G3 is $-\text{SO}_2-(\text{CH}_2)_x-\text{R}^{12}$ [(G3)],

G4 is



wherein

Ar^1 and

Ar^2 are selected independently of each other from the group consisting of phenyl, pyridyl and naphthyl; [,]

G5 is $-\text{COR}^{15}$ [(G5)],

wherein

R^{15} is selected from the group consisting of trifluoromethyl, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$ and benzyloxy; [,] and

wherein aromatic [ring systems optionally] rings are substituted or unsubstituted independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, phenyl, benzyl, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, and a substituted $\text{C}_1\text{-C}_6\text{-alkoxy}$ which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, $\text{C}_1\text{-C}_6\text{-alkylthio}$, carboxy, $\text{C}_1\text{-C}_6\text{-alkoxycarbonyl}$,

benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups [in the ring] of an aromatic ring in the substituted C1-C6 alkoxy [or ring system optionally] may form an additional ring over a methylenedioxy bridge.

44. (once amended) A compound according to claim 43 wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, methyl, trifluoromethyl, hydroxy, methoxy and methoxycarbonyl,

R² is hydrogen or halogen,

R³ is hydrogen,

R⁴ is selected from the group consisting of hydrogen, C₁-C₃-alkyl and hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₆-alkenylene, [optionally]

a substituted C₂-C₆-alkenylene which is substituted once or twice by hydroxy or fluorine, [or]

C₄-C₆-alkadienylene, [optionally]

a substituted C₄-C₆-alkadienylene which is substituted by one or two fluorine atoms, and

1,3,5-hexatrienylene

D is selected from the group consisting of C₂-C₈-alkylene,

[optionally]

a substituted C₂-C₈-alkylene which is substituted by methyl or hydroxy

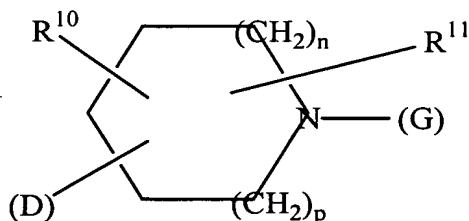
C₂-C₈-alkenylene, [optionally]

a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy, [wherein the double bond optionally is to ring E, and]

a substituted C₂-C₈-alkenylene which is substituted by methyl or hydroxy, wherein the double bond is to ring E, [and]

an isosterically replaced C₂ to C₈ group selected from the group consisting of C₂-C₈-alkylene and C₂-C₈-alkenylene, [wherein] the isosterically replaced C₂ to C₈ group having methylene units and one to three of the methylene units are isosterically replaced by O, NH, N(CH₃), N(COCH₃), N(SO₂CH₃) or CO,

E is

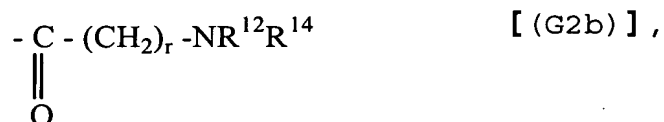
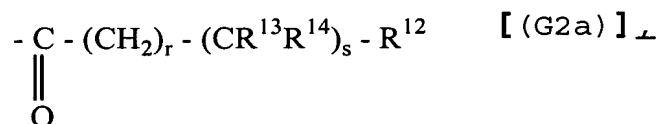
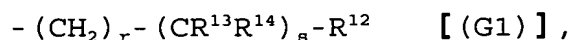


wherein **n** and **p** are, independent of each other, 0, 1, [or] 2, or 3, [with the proviso that] wherein **n + p** [= 2] ≤ 3,

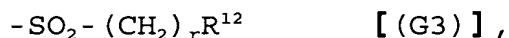
R¹⁰ is selected from the group consisting of hydrogen, methyl and hydroxyl,

R^{11} is hydrogen or an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, C₃-C₈-cycloalkyl, methoxycarbonyl, tert-butoxycarbonyl, benzyloxycarbonyl, trifluoroacetyl, diphenylphosphinoyl,



and



wherein

r is 0, 1 or 2,

s is 0 or 1,

R^{12} is selected from the group consisting of hydrogen, methyl, benzyl, phenyl, [the group consisting of] indanyl, indenyl, oxoindanyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, oxotetrahydronaphthyl, flourenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and oxodibenzocycloheptenyl, dihydrodibenzocycloheptenyl, oxodihydrodibenzocycloheptenyl bound directly or over a

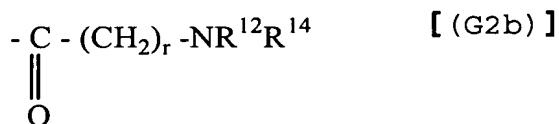
methylene group, [and the group consisting of] furyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, dihydrobenzofuryl, benzothienyl, dihydrobenzothienyl, indolyl, indolinyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzisoxazolyl, oxobenzisoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzoisothiazolyl, oxobenzoisothiazolyl, benzimidazolyl, oxobenzimidazolyl, benzofurazanyl, benzothiadiazolyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, isothiazolopyridyl, imidazopyridyl, oxodihydroimidazopyridyl, pyrazolopyridyl, thienopyrimidinyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, dihydroquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinoxalyl, quinazolyl, naphthyridinyl, carbazolyl, tetrahydrocarbazolyl, oxotetrahydrocarbazolyl, pyridoindolyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, oxobenzocycloheptathienyl, dihydrothienobenzothiepinyl, oxodihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, dihydropyridobenzoxepinyl, dihydrodibenzothiazepinyl, and oxodihydrodibenzothiazepinyl, bound directly or over a methylene group,

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl and phenyl,

R¹⁴ is selected from the group consisting of hydrogen,

hydroxy, methyl, benzyl, phenyl, [and the group consisting of] naphthyl, furyl, thienyl, oxazolyl, thiazolyl, pyrazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, benzofuryl, benzothienyl, indolyl, indolinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in formula



-NR¹²R¹⁴ [optionally is] may be selected from the group consisting of pyrrolidine, piperidine, (1H)-tetrahydropyridine, hexahydroazepine, octahydroazocine, piperazine, hexahydrodiazepine, morpholine, hexahydrooxazepine, 2-azabicyclo[2.2.1]heptane, 7-azabicyclo[2.2.1]heptane, 2,5-diazabicyclo[2.2.1]heptane, 8-azabicyclo[3.2.1]octane, 2,5-diazabicyclo[2.2.2]octane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydroquinoxaline, (4H)-dihydrobenzoxazine, (4H)-dihydrobenzothiazine, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indol, (10H)-dihydroacridine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (5H)-dihydrodibenzodiazepine, (11H)-dihydrodibenzo[b,e]oxazepine, (11H)-dihydrodibenzo[b,e]thiazepine, (10H)-dihydrodibenzo[b,f]oxazepine and (5H)-tetrahydrodibenzazocine,

wherein aromatic [ring systems are optionally] rings are substituted or unsubstituted independently of each other by

one to three substituents independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups [in the ring] of an aromatic ring in the substituted C₁-C₆ alkoxy [or ring system optionally] form an additional ring over a methylenedioxy bridge.

45. (once amended) A compound according to claim 22, wherein

R¹ is selected from the group consisting of hydrogen, fluorine, chlorine, bromine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0 or 1,

A is selected from the group consisting of C₂-C₄-alkenylene,

[or] 1,3-butadienylene, [which are optionally]
a C₂-C₄-alkenylene substituted by fluorine, and
a 1,3-butadienylene substituted by fluorine,

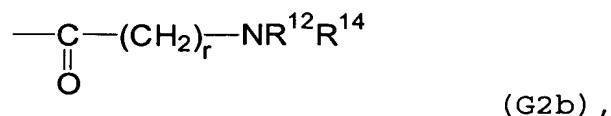
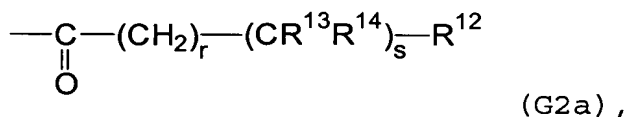
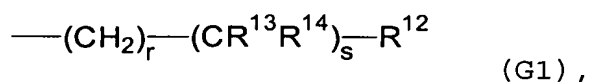
D is selected from the group consisting of C₂-C₆-alkylene, C₂-C₆-alkenylene,

C₂-C₆-alkylene and C₂-C₆-alkenylene wherein the double bond [optionally] is to ring E, and

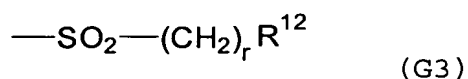
an isosterically replaced C2 to C6 group selected from the group consisting of C₂-C₆-alkylene and C₂-C₆-alkenylene, [wherein] the isosterically replaced C2 to C6 group having a methylene unit which is isosterically replaced by O, NH, N(CH₃) or CO, or an ethylene group which is isosterically replaced by NH-CO or CO-NH, or a propylene group which is isosterically replaced by NH-CO-O or O-CO-NH,

E is selected from the group consisting of piperidine, and a substituted piperidine wherein the heterocyclic ring [optionally] is substituted by an oxo group adjacent to the nitrogen atom,

G is selected from the group consisting of hydrogen, tert-butoxycarbonyl, diphenylphosphinoyl,



and



wherein

r is 0 or 1,

s is 0 or 1,

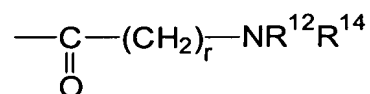
R¹² is selected from the group consisting of hydrogen, methyl, benzyl, phenyl, [the group consisting of] indenyl, oxoindanyl, naphthyl, tetrahydronaphthyl, fluorenyl, oxofluorenyl, anthryl, dihydroanthryl, oxodihydroanthryl, dioxodihydroanthryl, dibenzocycloheptenyl, and dihydrodibenzocycloheptenyl, bound directly or over a methylene group, [and the group consisting of] furyl, thienyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, imidazothiazolyl, benzofuryl, benzothienyl, indolyl, oxoindolinyl, dioxoindolinyl, benzoxazolyl, oxobenzoxazolyl, benzothiazolyl, oxobenzthiazolyl, benzimidazolyl, oxobenzimidazolyl, benzofurazanyl, benzotriazolyl, oxazolopyridyl, oxodihydrooxazolopyridyl, thiazolopyridyl, oxodihydrothiazolopyridyl, chromanyl, chromanonyl, benzopyranyl, chromonyl, quinolyl, isoquinolyl, oxodihydroquinolyl, tetrahydroquinolyl, oxotetrahydroquinolyl, benzodioxanyl, quinazolyl, acridinyl, oxodihydroacridinyl, phenothiazinyl, dihydrodibenzoxepinyl, benzocycloheptathienyl, dihydrothienobenzothiepinyl, dihydrodibenzothiepinyl, oxodihydrodibenzothiepinyl, dihydrodibenzazepinyl, oxodihydrodibenzazepinyl, octahydrodibenzazepinyl, benzocycloheptapyridyl, oxobenzocycloheptapyridyl, and

dihydrodibenzothiazepinyl, bound directly or over a methylene group,

R¹³ is selected from the group consisting of hydrogen, methyl, benzyl and phenyl,

R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl, [and the group consisting of] naphthyl, furyl, thienyl, pyridyl, benzofuryl, benzothienyl, indolyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, chromanyl, quinolyl and tetrahydroquinolyl, bound directly or over a methylene group,

wherein in the formula



(G2b)

—NR¹²R¹⁴ [optionally is] may be selected from

pyrrolidine, piperidine, hexahydroazepine, morpholine, 2,5-diazabicyclo[2.2.1]heptane, indoline, isoindoline, (1H)-dihydroquinoline, (1H)-tetrahydroquinoline, (2H)-tetrahydroisoquinoline, (1H)-tetrahydrobenzo[b]azepine, (1H)-tetrahydrobenzo[d]azepine, (5H)-tetrahydrobenzo[b]oxazepine, (5H)-tetrahydrobenzo[b]thiazepine, 1,2,3,4-tetrahydroacridanone, (5H)-dihydrodibenzazepine, (11H)-dihydrodibenzo[b,e]oxazepine and (11H)-dihydrodibenzo[b,e]thiazepine,

wherein aromatic rings [ring systems optionally] are substituted or unsubstituted, independently of each other, by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl,

trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups on the aromatic ring or ring system may [optionally] form an additional ring over a methylenedioxy bridge.

46. (once amended) A compound according to claim 45, wherein:

R¹ is selected from the group consisting of hydrogen, fluorine, methyl, trifluoromethyl and hydroxy,

R² and

R³ are hydrogen,

R⁴ is hydrogen or hydroxy,

k is 0,

A is ethenylene or 1,3-butadienylene

D is selected from the group consisting of C₂-C₆-alkylene, [or] C₂-C₆-alkenylene, a C₂-C₆-alkylene wherein the double bond [optionally] is to ring E, and a C₂-C₆-alkenylene wherein the double bond is to ring E.

E is selected from the group consisting of pyrrolidine, piperidine, hexahydroazepine and morpholine,

G is selected from the group consisting of benzyl, phenethyl, fluorenylmethyl, anthrylmethyl, diphenylmethyl, fluorenyl, dihydrodibenzocycloheptenyl,

furylmethyl, thienylmethyl, thiazolylmethyl, pyridylmethyl, benzothienylmethyl, quinolylmethyl, phenyl-thienylmethyl, phenyl-pyridylmethyl, dihydrodibenzoxepinyl, dihydrodibenzothiepinyl, acetyl, pivaloyl, phenylacetyl, diphenylacetyl, diphenylpropionyl, naphthylacetyl, benzoyl, naphthoyl, anthrylcarbonyl, oxofluorenylcarbonyl, oxodihydroanthrylcarbonyl, dioxodihydroanthrylcarbonyl, furoyl, pyridylcarbonyl, chromonylcarbonyl, quinolylcarbonyl, naphthylaminocarbonyl, dibenzylaminocarbonyl, benzylphenylaminocarbonyl, diphenylaminocarbonyl, indolinyl-1-carbonyl, dihydrodibenzazepin-N-carbonyl, tetrahydroquinolinyl-N-carbonyl, tetrahydrobenzo[b]azepinyl-N-carbonyl, methanesulfonyl, phenylsulfonyl, p-toluenesulfonyl, naphthylsulfonyl, quinolinsulfonyl, and diphenylphosphinoyl,

wherein aromatic rings [ring systems optionally] are substituted or unsubstituted independently of each other by one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkoxy, entirely or partially substituted by fluorine; benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups in the ring or ring system may [optionally] form an additional ring over a methylenedioxy bridge.

47. (once amended) A compound according to claim 4, which is selected from the group consisting of

N-[4-(1-methylsulfonylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-{4-[1-(2-naphthylsulfonyl)-piperidin-4-yl]-butyl}-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(1-naphthylaminocarbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide,

N-[4-(1-diphenylaminocarbonyl-piperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide,

N-{4-[1-(10,11-dihydrodibenzo[b,f]azepin-5-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, and

N-[4-(1-diphenylphosphinoyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide

or as a pharmaceutically acceptable acid addition salt thereof.

48. (once amended) A compound according to claim 42, which is selected from the group consisting of N-[4-(1-acetylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-[4-(1-diphenylacetyl-piperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(3,3-diphenylpropionyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-3-(pyridin-3-yl)-acrylamide, N-[4-(1-benzoylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-

pentadienoic acid amide, and N-{4-[1-(9-oxo-9H-fluoren-4-yl-carbonyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

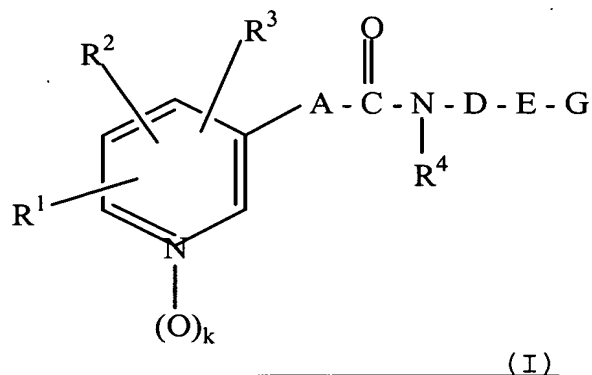
49. (once amended) A compound according to claim 42, which is selected from the group consisting of N-{4-[1-(phenylpyridin-3-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(phenylpyridin-4-yl-methyl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, N-{4-[1-(6,11-dihydrodibenzo[b,e]oxepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide and N-{4-[1-(6,11-dihydrodibenzo[b,e]thiepin-11-yl)-piperidin-4-yl]-butyl}-3-(pyridin-3-yl)-acrylamide, or as a pharmaceutically acceptable acid addition salt thereof.

50. (once amended) A compound according to claim 42, which is selected from the group consisting of N-[7-(1-diphenylmethylpiperidin-4-yl)-heptyl]-3-(pyridin-3-yl)-acrylamide, N-[8-(1-diphenylmethylpiperidin-4-yl)-octyl]-3-(pyridin-3-yl)-acrylamide, N-[3-(1-diphenylmethylpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide, and N-[3-(1-benzylpiperidin-4-yloxy)-propyl]-3-(pyridin-3-yl)-acrylamide or as a pharmaceutically acceptable acid addition salt thereof.

51. (once amended) A compound according to claim 42, which is selected from the group consisting of N-[2-(1-diphenylmethylpiperidin-4-yl)-ethyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[4-(1-diphenylmethylpiperidin-4-yl)-butyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide, N-[5-(1-diphenylmethylpiperidin-4-yl)-pentyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide and N-[6-(1-diphenylmethylpiperidin-4-yl)-hexyl]-5-(pyridin-3-yl)-2,4-pentadienoic acid amide or as a pharmaceutically acceptable

acid addition salt thereof.

56. (once amended) A pharmaceutical composition comprising one or more of the compounds according to formula (I) [claim 42 as active ingredient, optionally together with one or more pharmaceutically acceptable carriers, one or more toxicologically safe adjuvants, and optionally in combination with one or more other active ingredients] and pharmaceutically acceptable salts of formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR⁵R⁶, and bridged R¹R²; wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl; and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6 -alkyl, C_3-C_6 -alkenyl, hydroxy, C_1-C_6 -alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6 -alkenylene,

a substituted C_2-C_6 -alkenylene which is substituted one to three-fold by C_1-C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6 -alkadienylene,

a substituted C_4-C_6 -alkadienylene which is substituted once or twice by C_1-C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3 -alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of C_1-C_{10} -alkylene,

a substituted C_1-C_{10} -alkylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

C_2-C_{10} -alkenylene,

a substituted C_2-C_{10} -alkenylene which is substituted once

or twice by C₁-C₃-alkyl or hydroxy,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

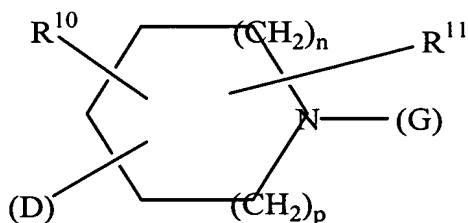
C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein n + p ≤ 3,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R¹¹ is selected from the group consisting of hydrogen

and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen,

G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of
hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles
which heterocycles contain one to three hetero-atoms selected
from the group consisting of N, S and O, which heterocycles
are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system with 8 to 16 ring atoms
and at least one aromatic ring and the carbocyclic ring and
aromatic ring being bonded with a bond which is either over an
aromatic or a hydrogenated ring and either directly or over a
methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring systems with 8 to 16
ring atoms and at least one aromatic ring, wherein one to
three ring atoms are selected from N, S and O and the
carbocyclic ring and aromatic ring being bonded with a bond

which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof;

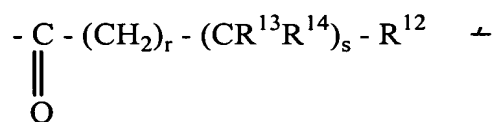
R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

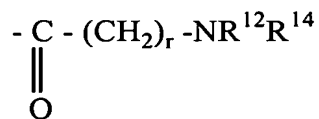
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

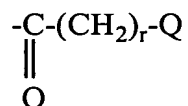
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



_____;

wherein R^{12} and R^{14} have the above meaning, and Q
is a nitrogen-containing heterocycle bound over the
nitrogen atom, the nitrogen-containing heterocycle being
selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-
membered heterocycles,

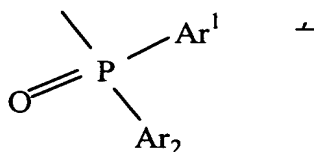
saturated and unsaturated monocyclic, four- to eight-
membered heterocycles, which, aside from an essential nitrogen
atom contain one or two further hetero-atoms selected from N,
S and O,

saturated and unsaturated bi- or tricyclic, anellated or
bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or
bridged heterocycles with 8 to 16 ring atoms, which, aside
from an essential nitrogen atom contain one or two further
hetero-atoms selected from N, S and O,

G3 is $-SO_2-(CH_2)_r-R^{12}$,

G4 is



wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is -COR¹⁵,

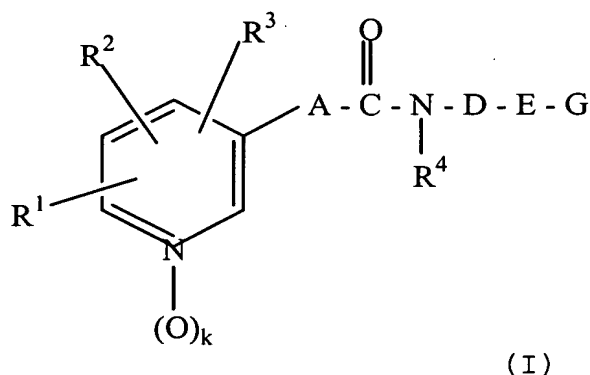
wherein

R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆-alkoxy may form an additional ring over a methylenedioxy bridge,

wherein general formula (I) does not include (E)-3-(3-pyridyl)-N-[2-(1-benzylpiperidin-4-yl)ethyl]-2-propenamide.

64. (once amended) A method of inhibiting tumor cell growth [treating cancer] in a [the] human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition [of claim 56] , wherein the pharmaceutical composition includes a compound of general formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR⁵R⁶, and bridged R¹R²; wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl; and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6 -alkyl, C_3-C_6 -alkenyl, hydroxy, C_1-C_6 -alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6 -alkenylene,

a substituted C_2-C_6 -alkenylene which is substituted one to three-fold by C_1-C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6 -alkadienylene,

a substituted C_4-C_6 -alkadienylene which is substituted once or twice by C_1-C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3 -alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of

C_1-C_{10} -alkylene,

a substituted C_1-C_{10} -alkylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

C_2-C_{10} -alkenylene,

a substituted C_2-C_{10} -alkenylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

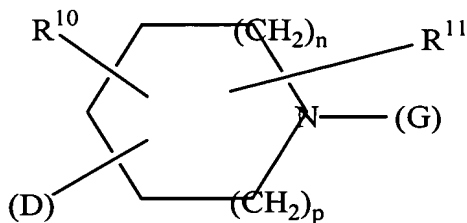
C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy,

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein n + p ≤ 3,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R¹¹ is selected from the group consisting of hydrogen and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen,
G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$
wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of
hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles
which heterocycles contain one to three hetero-atoms selected
from the group consisting of N, S and O, which heterocycles
are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system with 8 to 16 ring atoms
and at least one aromatic ring and the carbocyclic ring and
aromatic ring being bonded with a bond which is either over an
aromatic or a hydrogenated ring and either directly or over a
methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring systems with 8 to 16
ring atoms and at least one aromatic ring, wherein one to
three ring atoms are selected from N, S and O and the
carbocyclic ring and aromatic ring being bonded with a bond
which is either over an aromatic or a hydrogenated ring, and

either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof;

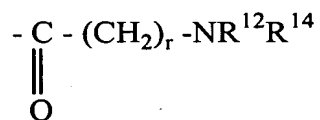
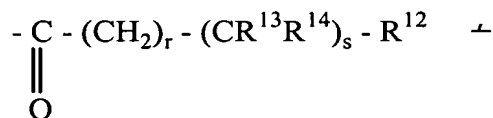
R¹⁴ is selected from the group consisting of hydrogen,
hydroxy,
methyl,
benzyl,
phenyl,

monocyclic aromatic five- and six-membered heterocycles
which contain one to three hetero-atoms selected from the
group consisting of N, S and O and are bound either directly
or over a methylene group,

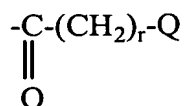
an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system with 8 to 16 ring atoms
and at least one aromatic ring and the carbocyclic ring and
the aromatic ring being bonded with a bond which is either
over an aromatic or a hydrogenated ring and either directly or
over a methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring system with 8 to 16
ring atoms and at least one aromatic ring, which heterocycles
contain one to three ring atoms are selected from N, S and O
and the heterocyclic ring and aromatic ring being bonded with
a bond which is over an aromatic or a hydrogenated ring and
either directly or over a methylene group;

G2 is selected from the group consisting of



and



_____;

wherein R^{12} and R^{14} have the above meaning, and Q
is a nitrogen-containing heterocycle bound over the
nitrogen atom, the nitrogen-containing heterocycle being
selected from the group consisting of

saturated and unsaturated monocyclic, four- to eight-
membered heterocycles,

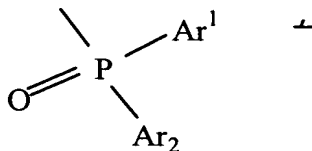
saturated and unsaturated monocyclic, four- to eight-
membered heterocycles, which, aside from an essential nitrogen
atom contain one or two further hetero-atoms selected from N,
S and O,

saturated and unsaturated bi- or tricyclic, anellated or
bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or
bridged heterocycles with 8 to 16 ring atoms, which, aside
from an essential nitrogen atom contain one or two further
hetero-atoms selected from N, S and O,

G3 is $\text{-SO}_2\text{-(CH}_2\text{)}_r\text{-R}^{12}$,

G4 is



wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl;

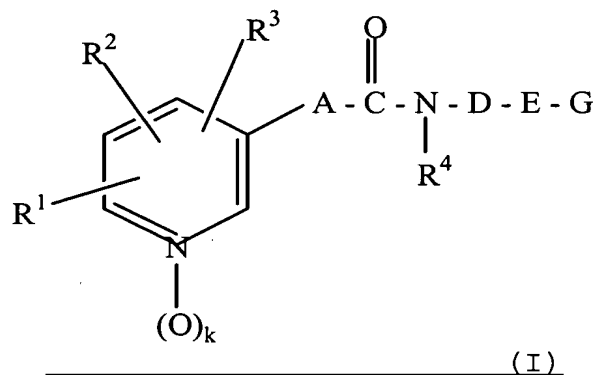
G5 is -COR¹⁵,

wherein

R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, Q, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₆-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, and a substituted C₁-C₆-alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge.

65. (Once amended) A method of suppressing autoimmune disease [immunoreactions] in [the] a human or animal body comprising administering to the human or animal body an effective amount of a pharmaceutical composition of [claim 56], wherein the pharmaceutical composition includes a compound of general formula (I) or a pharmaceutically acceptable salt of formula (I)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₄-hydroxyalkyl, hydroxy, C₁-C₄-alkoxy, benzyloxy, C₂-C₄-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, pyridyloxy, NR⁵R⁶, and bridged R¹R²; wherein

R⁵ is selected from the group consisting of hydrogen and C₁-C₆-alkyl; and

R⁶ is selected from the group consisting of hydrogen and C₁-C₆-alkyl;

R² is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and hydroxy and bridged R¹R²;

wherein

bridged R^1R^2 is where R^1R^2 are adjacent and form a bridge which is selected from the group consisting of $-(CH_2)_4-$, $-(CH=CH)_2-$ and $-CH_2O-CR^7R^8-O-$; wherein

R^7 is selected from the group consisting of hydrogen, and C_1-C_6 -alkyl; and

R^8 is selected from the group consisting of hydrogen and C_1-C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;

R^4 is selected from the group consisting of hydrogen, C_1-C_6 -alkyl, C_3-C_6 -alkenyl, hydroxy, C_1-C_6 -alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_2-C_6 -alkenylene,

a substituted C_2-C_6 -alkenylene which is substituted one to three-fold by C_1-C_3 -alkyl, hydroxy, fluorine, cyano, or phenyl,

C_4-C_6 -alkadienylene,

a substituted C_4-C_6 -alkadienylene which is substituted once or twice by C_1-C_3 -alkyl, fluorine, cyano, or phenyl, 1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C_1-C_3 -alkyl, fluorine, or cyano, and ethynylene;

D is selected from the group consisting of C_1-C_{10} -alkylene,

a substituted C_1-C_{10} -alkylene which is substituted once or twice by C_1-C_3 -alkyl or hydroxy,

C_2-C_{10} -alkenylene,

a substituted C_2-C_{10} -alkenylene which is substituted once

or twice by C₁-C₃-alkyl or hydroxy.

a substituted C₂-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy, wherein the double bond is to E,

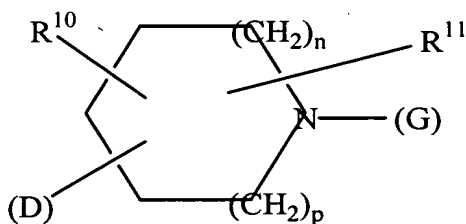
C₃-C₁₀-alkynylene,

a substituted C₃-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy.

an isosterically replaced C₁ to C₁₀ group selected from the group consisting of C₁-C₁₀-alkylene, C₂-C₁₀-alkenylene and C₃-C₁₀-alkynylene, the isosterically replaced C₁ to C₁₀ group having methylene units and one to three of the methylene units are isosterically replaced by O, S, NR⁹, CO, SO or SO₂; wherein

R⁹ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, C₂-C₆-acyl and methanesulfonyl;

E is



wherein n and p are, independent of each other, 0, 1, 2, or 3 wherein n + p ≤ 3,

R¹⁰ is selected from the group consisting of hydrogen, C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy and C₂-C₇-alkoxycarbonyl;

R¹¹ is selected from the group consisting of hydrogen

and an oxo group adjacent to the nitrogen atom in E;

G is selected from the group consisting of hydrogen,

G1, G2, G3, G4 and G5; wherein

G1 is $-(CH_2)_r-(CR^{13}R^{14})_s-R^{12}$

wherein

r is 0, 1 or 2, and

s is 0 or 1,

R¹² is selected from the group consisting of
hydrogen,

C₁-C₆-alkyl,

C₃-C₆-alkenyl,

C₃-C₆-alkinyl,

C₃-C₈-cycloalkyl,

benzyl,

phenyl,

monocyclic aromatic five- and six-membered heterocycles
which heterocycles contain one to three hetero-atoms selected
from the group consisting of N, S and O, which heterocycles
are bound directly to or over a methylene group,

an anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring system with 8 to 16 ring atoms
and at least one aromatic ring and the carbocyclic ring and
aromatic ring being bonded with a bond which is either over an
aromatic or a hydrogenated ring and either directly or over a
methylene group, and

a N, S, O anellated bi- and tricyclic aromatic or
partially hydrogenated heterocyclic ring systems with 8 to 16
ring atoms and at least one aromatic ring, wherein one to
three ring atoms are selected from N, S and O and the
carbocyclic ring and aromatic ring being bonded with a bond

which is either over an aromatic or a hydrogenated ring, and either directly or over a methylene group;

R¹³ has the same meaning as R¹², but is selected independently thereof;

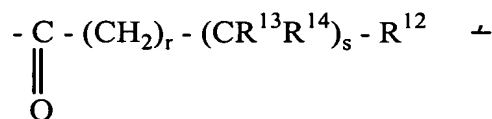
R¹⁴ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

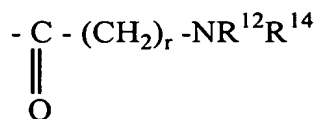
monocyclic aromatic five- and six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O and are bound either directly or over a methylene group,

an anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring and the carbocyclic ring and the aromatic ring being bonded with a bond which is either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

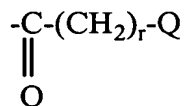
a N, S, O anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring system with 8 to 16 ring atoms and at least one aromatic ring, which heterocycles contain one to three ring atoms are selected from N, S and O and the heterocyclic ring and aromatic ring being bonded with a bond which is over an aromatic or a hydrogenated ring and either directly or over a methylene group;

G2 is selected from the group consisting of





and



_____;

wherein R^{12} and R^{14} have the above meaning, and Q is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle being selected from the group consisting of saturated and unsaturated monocyclic, four- to eight-membered heterocycles,

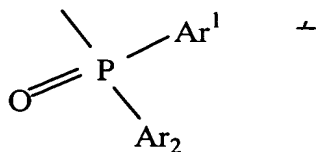
saturated and unsaturated monocyclic, four- to eight-membered heterocycles, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms;

saturated and unsaturated bi- or tricyclic, anellated or bridged heterocycles with 8 to 16 ring atoms, which, aside from an essential nitrogen atom contain one or two further hetero-atoms selected from N, S and O,

G3 is $-SO_2-(CH_2)_r-R^{12}$,

G4 is



wherein

Ar¹ is selected from the group consisting of phenyl, pyridyl and naphthyl; and

Ar² is selected from the group consisting of phenyl, pyridyl and naphthyl;

G5 is -COR¹⁵,

wherein

R¹⁵ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy and benzyloxy; and

wherein aromatic rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, O, Ar¹ and Ar² are unsubstituted or substituted, the substituted rings in R¹, R⁴, R¹², R¹³, R¹⁴, R¹⁵, O, Ar¹ and Ar² having one to three substituents which are independently selected from the group consisting of halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, C₃-C₈-cycloalkyl, phenyl, benzyl, hydroxy, C₁-C₆-alkoxy, C₁-C₆-alkoxy, and a C₁-C₆ alkoxy which is entirely or partially substituted by fluorine, benzyloxy, phenoxy, mercapto, C₁-C₆-alkylthio, carboxy, C₁-C₆-alkoxycarbonyl, benzyloxycarbonyl, nitro, amino, mono-C₁-C₆-alkylamino, and di-(C₁-C₆-alkyl)-amino, wherein two adjacent groups of an aromatic ring in the substituted C₁-C₆ alkoxy may form an additional ring over a methylenedioxy bridge.